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Structural and Qualitative Analysis of Lamotrigine

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Abstract

In the present study, the change in the quality of lamotrigine that falls under antiepileptic group at various storage conditions has been studied by FTIR and UV spectroscopic technique. The indications from the result emphasizes that it is essential to store the drugs under the prescribed condition to maintain their quality. The Vibrational spectral analysis also been carried out by employing FTIR, FT-Raman spectroscopy.

Keyword: Lamotrigine; FTIR; FT –Raman; UV spectroscopy

Introduction

A drug is a substance used in diagnosis, treatment or prevention of a disease or as a component of a medication used as a medicine which kills or inactivates germs that affects body function or origin. World health organization states epilepsy as the third most common neurological disease in the world after Alzheimer's and Stroke. Taking this factor a detailed study on qualitative analysis using FTIR and UV spectroscopy and structural analysis using FTIR and FT Raman spectroscopy and has been carried on lamotrigine an antiepileptic drug chemically known as 6-(2, 3-dichlorophenyl)-1 2,4-triazine-3,5-diamine with a molecular formula $C_9H_7Cl_2N_5$. To investigate the structure and analysis of pharmaceutical active compounds spectroscopic techniques have been widely used in the recent past. Gunasekaran et al. [1-8] have done the qualitative analysis and structural confirmation on drugs using FTIR and UV spectroscopy.

Experimental

The spectroscopically pure grade sample of lamotrigine was purchased from a reputed Pharmaceutical company, Chennai, India and was used as such for the spectral measurements. FTIR spectrum of lamotrigine has been recorded in the range 4000 - 450 cm^{-1} in the solid state by adopting the KBr pellet technique and FT-Raman spectrum has been recorded in the range 4000 - 50 cm^{-1} using laser wave number 15,798 cm-1 as excitation sources on a computer interfaced BRUKER IFS 66V model Interferometer at IITM, Chennai. UV spectral measurements have been made using Cary 5E –UV-VIS spectrophotometer in the wavelength region 200-400 nm at IIT, Chennai. All sharp bands observed in the spectra are expected to have an accuracy of ±1cm-1.

Result and Discussion

Vibrational assignment

Infrared and Raman spectra contain a number of bands at specific wave numbers. The aim of the vibrational analysis is to decide which of the vibrational modes give rise to each of these observed bands. The molecule lamotrigine has 23 atoms and possess C_1 symmetry configuration. The molecular structure of lamotrigine is shown in Figure 1.The assignments for the fundamental modes of vibrations have been made on the basis of the position shape and intensity. The FTIR and FT- Raman spectra of lamotrigine were shown in Figures 2 and 3. The observed FTIR and FT-Raman frequencies for selected modes of vibrations for lamotrigine are presented in Table 1.

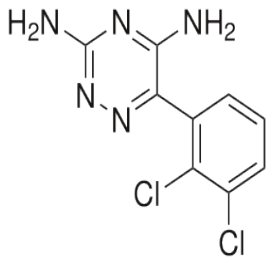

Figure 1: Molecular structure of lamotrigine.

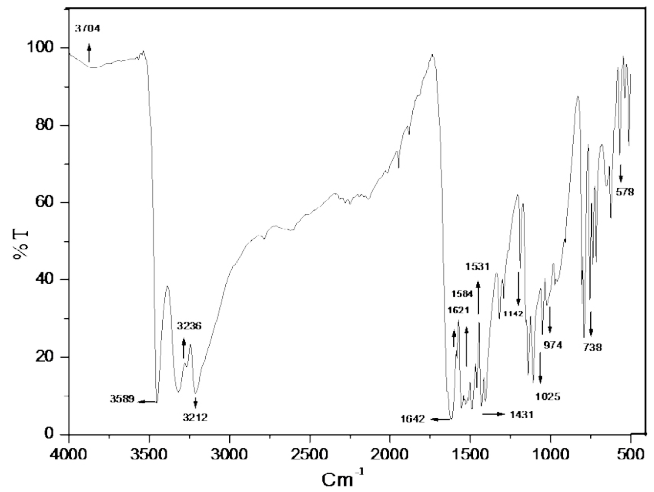

Figure 2: FTIR Spectrum of lamotrigine.

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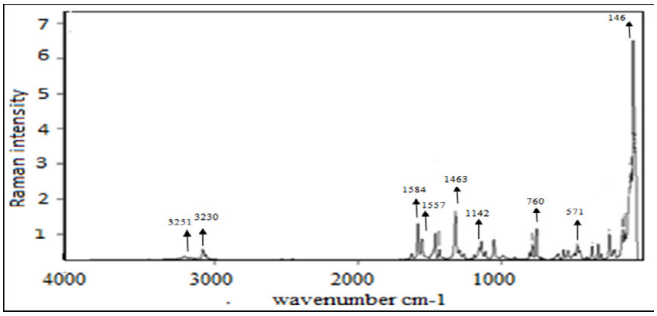

Figure 3: FT -Raman Spectrum of lamotrigine.

Frequency cm^{-1}		
FTIR	FT Raman	Band Assignment
-	146	C-C Twisting
-	210	C-Cl Scissoring
-	215	C-N Wagging
-	331	CCC in plane deformation
-	372	NH_2 Rocking
-	474	NH_2 Rocking
578	571	C-Cl Stretching +NH_2twisting
624	-	C-Cl Stretching +Aromatic ring Stretching
717	-	C-Cl Stretching+C-N Stretching
738	-	C-Cl Stretching +C-C-C in plane bending
756	760	CNC Stretching + NH_2 Rocking
908	-	Aromatic Deformation
974	-	Aromatic Deformation + NH_2Rocking
1025	-	NH_2Rocking+Aromatic C-H in Plane Bending
1142	1142	Aromatic Breathing + NH_2Rocking
1221	-	Aromatic Deformation
1292	-	CC Stretching + C=N Stretching
1431	1434	C- C Stretching
1460	1463	C=N Stretching+C-H Stretching
1489	-	C-H Aromatic ring Stretching
1531	1557	C-C Stretching+C=N Stretching+NH2 Scissoring
1584	1584	Aromatic C-C Stretching + NH_2 scissoring
1621	-	Aromatic breathing + NH_2Scissoring
1642	1639	C=N Stretching +NH2Scissoring
3204	-	C-H Asym. Stretching
3212	3230	C-H Asym. Stretching
3236	3251	C-H Sym.Stretching
3589	-	NH_2 Symmetric Stretching
3672	-	NH_2Symmetric Stretching
3704	-	NH_2Asymmetric Stretching
3741	-	NH_2 Asymmetric Stretching

Table 1: Vibrational assignment for lamotrigine.

NH_2 Group vibrations

The NH_2 groups in the sample under investigation give rise to two symmetric and two asymmetric stretching vibrations. The frequency of asymmetric vibration is higher than that of symmetric one. It has frequency range of 3300 cm^{-1} to 3700 cm^{-1} [9]. In addition, NH_2 group has scissoring, rocking, wagging modes. The NH_2 scissoring mode has been suggested to lie in the region 1550 cm-1 to 1650 cm^{-1}. In the present work NH_2 scissoring band occurs at 1531, 1584, 1621, 1642 cm^{-1} in the FTIR spectrum and at 1557, 1584, 1639cm^{-1} in FT -Raman spectrum. Similarly NH_2 rocking vibration occurs at 1142 cm^{-1} in the FTIR and FT- Raman spectrum respectively. NH_2 twisting vibration occurs at 571cm^{-1} and corresponding Raman band is observed at 571 cm^{-1}.

C-Cl Vibrations

The C-Cl stretching vibrations give generally strong bands in the region 710-505 cm^{-1} [10]. Compounds with more than one chlorine atom exhibit very strong bands due to the asymmetric and symmetric stretching modes. Hence in the present investigation the bands at 578,624,717,738cm^{-1} in FTIR spectrum and 571cm^{-1} in the FT- Raman spectrum are assigned to the C-Cl stretching Vibrational mode. The band at 210cm^{-1} in the FT- Raman spectrum corresponds to the C-Cl scissoring mode.

C=N vibrations

The ring C=N stretching vibrations [11] occur in the region 1645-1575 cm^{-1}.S. Gunasekaran and Leela Abraham [12] have observed the C=N stretching band at 1612 cm^{-1} in benzocaine. Referring to the above assignments the bands at1531, 1584 and 1642cm^{-1} in FTIR and 1557, 1584cm^{-1} in FT Raman spectrum in lamotrigine are assigned to C=N symmetric and asymmetric stretching vibrations respectively.

Aromatic vibrations

The aromatic C-H stretching vibrations generally appear in the region 3000-3250cm^{-1} in substituted benzenes [13]. Many researchers reported the C-H stretching frequency for the benzene derivatives are in this region. Considering this, in the present case, the bands at 3204, 3212cm-1 in FTIR and 3230cm^{-1}in FT Raman are assigned to C-H asymmetric stretching vibrations in lamotrigine. The bands observed at3236cm^{-1}in FTIR and 3251cm^{-1} in FT Raman are assigned to C-H symmetric stretching for the same molecule. The Vibrational bands at 1142cm-1 corresponds to aromatic breathing and1052cm-1 and 1054cm-1 are assigned to aromatic C-H in plane bending in FTIR and FT Raman spectrum respectively. The band at 1221cm-1 in the FTIR spectrum corresponds to aromatic deformation.

Qualitative analysis

Drug quality is a source of great concern worldwide as pharmaceutical products plays an important role in improving the health and promoting the well being of every individual. Use of poor quality drugs has serious health implications and wasted resources. Temperature is one of the important environmental parameter that plays a key role in maintaining the drug quality. Drug must be stored, handled and transported according to predetermined conditions as supported by stability data. Drugs which are not stored under the recommended temperature conditions might degrade even prior to the expiration date. Among the various methods for the analysis, spectroscopic techniques are a predominant tool used to analyze the quality of drugs under different storage conditions. In the present work FTIR and UV spectroscopic methods have been applied to check the nature and the quality of the drug sample lamotrigine when it is exposed to sunlight, ice point etc.,

The FTIR overlay spectra and the corresponding absorbance of the drug have been recorded when stored under prescribed condition as per the guidelines of Indian Pharmacopeia, exposed to sunlight (50°

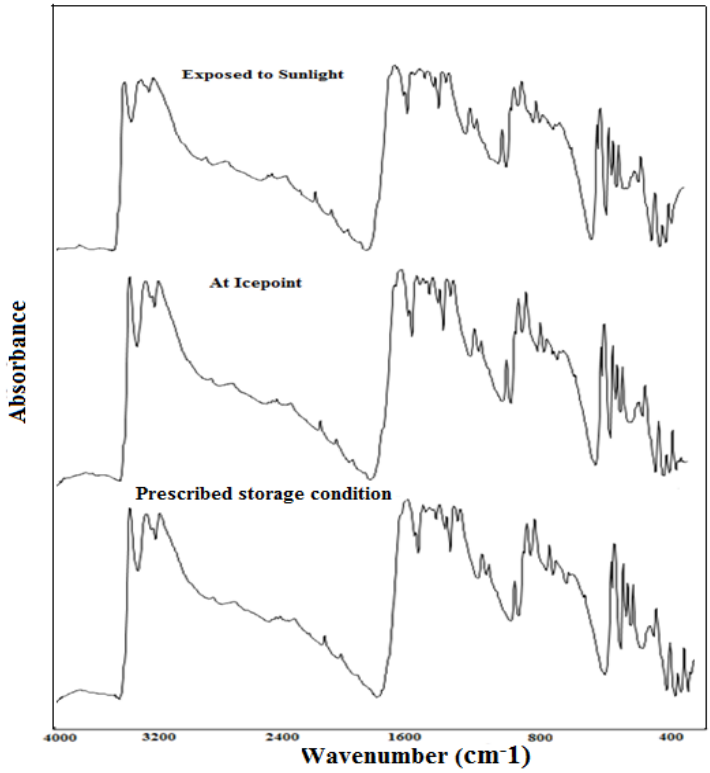

Figure 4: Overlay spectrum of lamotrigine stored at different condition.

Wave number (cm^{-1})	Absorbance		
	Prescribed storage condition	Ice point	Exposed to Sunlight
3451	0.9184	0.9234	0.8698
3317	0.8904	0.9060	0.8781
3212	0.8938	0.9068	0.8938
2136	0.3905	0.3539	0.3891
1584	0.8032	0.7754	0.8241
1556	0.9309	0.9305	0.8500
1431	0.9272	0.9170	0.9274
1109	0.8669	0.8578	0.8769
624	0.4389	0.4295	0.4784

Table 2: Absorbance for certain modes of vibration under different conditions of storage for lamotrigine.

C) and maintained at ice point (0°C) and are presented in Figure 4 and Table 2 which clearly indicates change in the absorbance values with change in storage condition.

The internal standard ratio is calculated among the various absorption modes of vibration of the drug and the results are tabulated in Table 3. The internal standard ratios evaluated clearly shows the deterioration in the quality of the sample due to alteration in the storage conditions.

The result obtained by FTIR study has been confirmed by UV spectral studies. The UV spectrum of the sample in pure form and at different storage conditions has been recorded to identify the variation in the wavelength maximum (λ_{max}) and is tabulated in Table 4. The UV spectrum of lamotrigine at different storage conditions is presented in the Figure 5. It is inferred from the result obtained, that the quality will definitely alter when it is kept under the unprescribed environmental conditions.

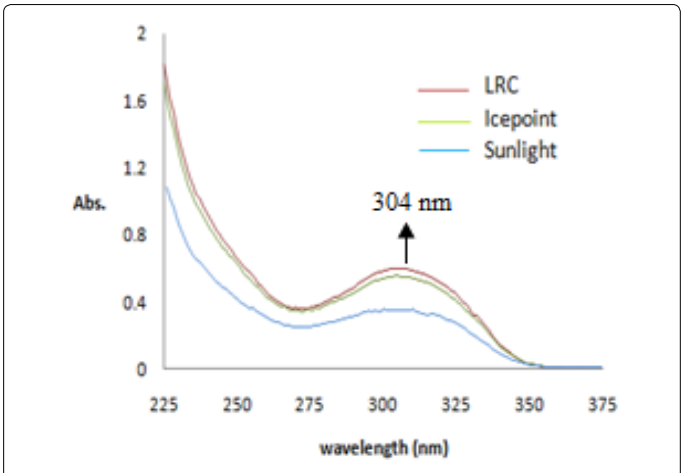

Figure 5: UV spectrum of lamotrigine.

Condition of Exposure	Internal Standard of specific modes of vibration at 3451cm^{-1}								
	A3451/3451	**A3317/3451**	**A3212/3451**	**A2136/3451**	**A1584/3451**	**A1556/3451**	**A1431/3451**	**A1109/3451**	**A624/3451**
Prescribed storage condition	1.0000	0.9695	0.9732	0.4251	0.8745	1.0136	1.0095	0.9439	0.4778
At ice point	1.0000	0.9811	0.9811	0.3832	0.8397	1.0076	0.993	0.9289	0.4651
Exposed to sunlight	1.0000	1.0095	1.0275	0.4473	0.9474	0.9772	1.0662	1.0081	0.55
Condition of Exposure	**Internal Standard of specific modes of vibration at 3317cm^{-1}**								
	A3451/3317	**A3317/3317**	**A3212/3317**	**A2136/3317**	**A1584/3317**	**A1556/3317**	**A1431/3317**	**A1109/3317**	**A624/3317**
Prescribed storage condition	1.0314	1.0000	1.0038	0.4385	0.902	1.0454	1.0413	0.9736	0.4929
At ice point	1.0192	1.0000	0.9811	0.3906	0.8558	1.027	1.0121	0.9467	0.474
Exposed to sunlight	0.9905	1.0000	1.0275	0.4431	0.9385	0.9679	1.0561	0.9986	0.5448
Condition of Exposure	**Internal Standard of specific modes of vibration at 3212cm^{-1}**								
	A3451/3212	**A3317/3212**	**A3212/3212**	**A2136/3212**	**A1584/3212**	**A1556/3212**	**A1431/3212**	**A1109/3212**	**A624/3212**
Prescribed storage condition	1.0275	0.9961	1.0000	0.4368	0.8986	1.0415	1.0373	0.9699	0.491
At ice point	1.0183	0.9991	1.0000	0.3902	0.855	1.0261	1.0112	0.9459	0.4736
Exposed to sunlight	0.9731	0.9824	1.0000	0.4353	0.922	0.9509	1.0375	0.981	0.5352
Condition of Exposure	**Internal Standard of specific modes of vibration at 2136cm^{-1}**								
	A3451/2136	**A3317/2136**	**A3212/2136**	**A2136/2136**	**A1584/2136**	**A1556/2136**	**A1431/2136**	**A1109/2136**	**A624/2136**
Prescribed storage condition	2.3518	2.2801	2.2888	1.0000	2.0568	2.3838	2.3743	2.2199	1.1239
At ice point	2.6092	2.56	2.5623	1.0000	2.191	2.6292	2.5911	2.4238	1.2136
Exposed to sunlight	2.2354	2.2567	2.297	1.0000	2.1179	2.1845	2.3834	2.2536	1.2295
Condition of Exposure	**Internal Standard of specific modes of vibration at 1584cm^{-1}**								
	A3451/1584	**A3317/1584**	**A3212/1584**	**A2136/1584**	**A1584/1584**	**A1556/1584**	**A1431/1584**	**A1109/1584**	**A624/1584**
Prescribed storage condition	1.1434	1.1085	1.1127	0.4861	1.0000	1.1589	1.1543	1.0793	0.5464
At ice point	1.1908	1.1684	1.1694	0.4564	1.0000	1.2	1.1826	1.1062	0.5539
Exposed to sunlight	1.0554	1.0655	1.0845	0.4721	1.0000	1.0314	1.1253	1.064	0.5805
Condition of Exposure	**Internal Standard of specific modes of vibration at 1556cm-1**								
	A3451/1556	**A3317/1556**	**A3212/1556**	**A2136/1556**	**A1584/1556**	**A1556/1556**	**A1431/1556**	**A1109/1556**	**A624/1556**
Prescribed storage condition	0.9865	0.9564	0.9601	0.4194	0.8628	1.0000	0.996	0.9312	0.4714
At ice point	0.9923	0.9736	0.9745	0.3803	0.8333	1.0000	0.9854	0.9218	0.4615
Exposed to sunlight	1.0232	1.033	1.0515	0.4577	0.9695	1.0000	1.091	1.0316	0.5628
Condition of Exposure	**Internal Standard of specific modes of vibration at 624cm^{-1}**								
	A3451/624	**A3317/624**	**A3212/624**	**A2136/624**	**A1584/624**	**A1556/624**	**A1431/624**	**A1109/624**	**A624/624**
Prescribed storage condition	2.0925	2.0287	2.0364	0.8897	2.1209	2.104	2.1125	1.9751	1.0000
At ice point	2.1499	2.1094	2.1112	0.8239	1.8053	2.1664	1.135	1.9972	1.0000
Exposed to sunlight	1.8181	1.8354	1.8683	0.8133	1.7226	1.7767	1.9385	1.8329	1.0000

Table 3: Internal standard evaluation for lamotrigine.

Storage condition	Absorbance at λ_{max} =304 nm
Light Resistance Container(LRC)	0.5996
Ice point	0.5538
Sunlight	0.3537

Table 4: lamotrigine stored at different conditions.

Conclusion

A satisfactory Vibrational assignment of the drug with the FTIR and FT- Raman spectra recorded confirms the basic functional groups present in the lamotrigine. FTIR and UV spectroscopic technique have been employed for the qualitative analysis of lamotrigine. The FTIR and UV spectrum recorded clearly denotes the change in the absorbance values with storage condition emphasizing the fact that the drug should always be kept under the guidelines provided for storage to maintain their quality.

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